

Is the global rise of asthma an early impact of anthropogenic climate change?

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doi:10.1289/ehp.7724 (available at <http://dx.doi.org/>)
Online 20 April 2005



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Running title

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Acknowledgments

A conflict of interest was not reported. Many thanks to Professor Neil Pearce for providing asthma prevalence data, and to the National Centre for Epidemiology and Population Health review group for their very helpful comments: Dr Charles Blumer, Dr Rennie D'Souza, Dr Kathryn Glass, Mr James Harris, Dr Robyn Lucas, Dr Lyndall Strazdins and Dr Rosalie Woodruff.

Key words

aeroallergens

anthropogenic climate change

asthma

carbon dioxide

phenology

pollen

temperature

Abbreviations

CO₂: carbon dioxide

DJF: December, January, February

IPCC: Intergovernmental Panel on Climate Change

ISAAC: International Study of Asthma and Allergies in Childhood

MAM: March, April, May

JJA: June, July, August

ppm: parts per million

SON: September, October, November

Th1: T helper type 1

Th2: T helper type 2

WHO: World Health Organization

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Abstract

The increase in asthma incidence, prevalence and morbidity over recent decades presents a significant challenge to public health. Pollen is an important trigger of some types of asthma and both pollen quantity and season are dependent on climatic and meteorological variables. Over the same period as the global rise in asthma there have been considerable increases in atmospheric carbon dioxide concentration and global average surface temperature. We hypothesize anthropogenic climate change as a plausible contributor to the rise in asthma. Greater concentrations of carbon dioxide and higher temperatures may increase pollen quantity, and induce longer pollen seasons. Pollen allergenicity can also increase as a result of these changes in climate. Exposure in early life to a more allergenic environment may also provoke the development of other atopic conditions, such as eczema and allergic rhinitis. Although the etiology of asthma is complex, the recent global rise in asthma could be an early health effect of anthropogenic climate change.

Global trends in asthma

Although asthma patterns vary throughout the world, considerable increases in both the prevalence of asthma and its severity have occurred globally over recent decades (Bach 2002; Isolauri et al. 2004; Pearce et al. 2000). As this rise has been far too rapid to implicate any genetic basis for change, various environmental factors and lifestyle factors have been proposed, and most recently, the 'hygiene hypothesis' has been explored extensively (Bach 2002) as an explanation for increased asthma prevalence. In this paper we propose an additional explanation: that a significant proportion of the increase in both asthma prevalence and its severity is the result of anthropogenic climate change.

Evidence for the global increase in the burden of asthma has come from studies of incidence, prevalence, and morbidity. Asthma prevalence appears to have increased since the early 1960s (Beasley 2002) with the rise in asthma prevalence occurring among both children and adults (Beasley et al. 2000) and in a wide range of countries with differing lifestyles (Beasley 2002). Over a similar period, the prevalence of other atopic disorders, such as allergic rhinitis, atopic eczema, and urticaria, has also increased, once again throughout the world (Bach 2002; Beasley 2002). Figure 1 shows increasing prevalence of asthma in several locations. Although different diagnostic definitions have been used in different locations, each location shown is internally consistent, and each shows an increase in asthma prevalence.

Figure 1 about here

Studies of hospital admissions and surveys of symptoms of severe asthma indicate increased asthma morbidity since the early 1960s (Beasley 2002; Kao et al. 2001; Kerr 2002), particularly in young children (Beasley 2002). This increase in asthma morbidity can not be completely

explained by an increase in re-admissions, diagnostic transfer from related disease categories, or changes in medical practice (Beasley 2002).

In contrast to the overall trend of a rise in asthma over several decades, a few studies have reported an apparent leveling off or even a decline of asthma in recent years. Robertson et al. (2004) reported a 26% decline in the prevalence of reported wheeze between surveys conducted in 1993 and 2002 in Melbourne, Australia, among children aged 6 to 7 years. The study also found a reduction in emergency room visits and hospital admissions, which may be at least in part due to improved asthma management. Interestingly the same survey found a 31% increase in allergic rhinitis, which is commonly linked to asthma, and a 55% increase in eczema, and an increase in those taking regular steroid medication among those with frequent wheeze. A UK study comparing reported wheeze in 12-14 year olds in 1995 and 2002 (Anderson et al. 2004) also found a decrease in reported prevalence of wheezing, and a decline in frequency and severity of attacks, but the proportion reporting that they had ever had asthma increased by 26% (allergic rhinitis by 8%). Both of these studies infer trends from only two time points. Although this is not uncommon where good data are scarce, care is required in their interpretation.

Fleming et al. (2000) examined weekly GP returns in England and Wales between 1989 and 1998. Following a peak in 1993/94, there appears to have been a gradual decline in new asthma presentations to GPs, which is mirrored by a similar decline in acute bronchitis presentations. This study benefits from having continuous (weekly) data available over a decade rather than two points in time. Nevertheless, the observed decline occurred only over four to five years, which is a relatively short time in a half century of overall observed increase. Recent milder winters (perhaps due to climate change) may have contributed to this decline, although some decrease was observed in other seasons (Fleming et al. 2000).

Furthermore, although new presentations declined, there was no reduction in the use of bronchodilators, and the use of inhaled steroids increased during the same period.

If the plateaus in asthma prevalence recently observed in these studies are real and prove to be sustained, this could be an indication that saturation point has been reached in some locations. With heritability estimated to be up to 75%, there is likely to be some genetic component in the etiology of asthma. Recent plateaus may reflect that the proportion of the population genetically more susceptible to developing asthma may already have done so. Further, there are a number of co-occurring factors that may promote a decline in asthma, exerting perhaps converse pressure protecting against asthma, for instance increases in the number of children attending childcare (see 'hygiene hypothesis' below).

There has been a sustained focus on identifying the causative environmental factors of the overall trend to increasing asthma prevalence and morbidity (Sunyer et al. 1999); however, these environmental factors are still unknown (Nolte et al. 2001). Some environmental factors previously proposed to explain the increased global prevalence of asthma include increased air pollution (D'Amato et al. 2000; Rios et al. 2004), changed diet (Ellwood et al. 2001; Hijazi et al. 2000; Seaton and Devereux 2000; Sigurs et al. 1992), and increased prevalence of maternal smoking (Lødrup Carlsen 2002; Ulrik and Backer 2000). Further potential explanatory factors come under the 'hygiene hypothesis', which proposes that greater risk of atopy results from altered challenges to the immune system in early life – in particular reduced infections – and the consequent development of a bias towards T helper type 2 (Th2) immune response over T helper type 1 (Th1) (Strachan 2000a). Specific factors proposed under the hygiene hypothesis include changed immunization practices (Portengen et al. 2002; von Mutius 1998), changed living conditions and increased exposure to indoor allergens (Kaiser 2004), increased use of antibiotics (Cohet et al. 2004; Droste et al. 2000;

Foliaki et al. 2004), and reduced exposure to endotoxins (Eder and von Mutius 2004; Eduard et al. 2004; Gehring et al. 2001). These factors may explain some of the increase in predisposition to atopy, but any effects on asthma prevalence and morbidity could be compounded by changing pollen profiles. Furthermore, studies examining the hygiene hypothesis have not been entirely consistent, with some showing no effects of these exposures on subsequent development of asthma (von Hertzen and Haahtela 2004). Inconsistencies may result from different social trends that alter exposures in more than one direction. While some trends may have reduced potentially protective exposures (increased urbanization, reduced family size, and increased maternal work stress during pregnancy), others (such as greater use of formal childcare) may serve to increase the protective exposures.

Climate change provides an additional plausible explanation for both increasing asthma susceptibility and increasing severity observed over several decades. There are many types of asthma, and we seek to explain only the component of the increase which is allergic asthma, and pollen-induced asthma in particular. This is likely to be a significant proportion of asthma cases. For example, Grossman (1997) suggests that up to 78% of people with asthma also suffer from allergic rhinitis. Furthermore, while the hypothesis that trends in air pollution have been major determinants for the rise in prevalence of asthma and allergic disease in recent decades is now generally disproved (Charpin et al. 1999; Strachan 2000b), air pollution is likely to have its own effects on pollen production (D'Amato et al. 2001).

Anthropogenic climate change

Human activities have led to increases in atmospheric carbon dioxide (CO₂) concentration and consequent changes in climate (IPCC 2001). Before the Industrial Era (circa 1750) atmospheric CO₂ concentration was 280 ± 10 parts per million (ppm) for several thousand

years (Prentice et al. 2001). It has risen since then, with the mean annual concentration recorded at the Mauna Loa Observatory in Hawaii in 2002 at 373 ppm (Keeling and Whorf 2003) (Figure 2). The increase over this period has not been linear. The Mauna Loa data show an 18% increase in the mean annual concentration since the start of the records in 1959, when it was 316 ppm (Keeling and Whorf 2003). This suggests approximately two-thirds of the increase in atmospheric CO₂ concentration since the Industrial Era has occurred over the last 50 years or so. These increases in CO₂ and other greenhouse gases have enhanced the greenhouse effect, resulting in global warming and other changes to climate. The global average surface temperature has increased by 0.6 ± 0.2 °C since the late 19th century, with much of this warming during two periods, 1910 to 1945 and 1976 to 2000 (Albritton et al. 2001). The Intergovernmental Panel on Climate Change has stated that “most of the observed warming over the last 50 years is likely to have been due to the increase in greenhouse gas concentrations” (Albritton et al. 2001). In addition to these already observed changes, human influences will continue to change atmospheric composition (including increasing CO₂) and climate throughout the 21st century and beyond (Albritton et al. 2001).

Figure 2 about here

Some researchers have proposed that global climate change is likely to have an effect in the future on asthma (Longstreth 1991). We suggest that some of the observed increase in asthma could be due to climate change that has already occurred.

Elevated CO₂ and climate change impacts on pollen

The balance of evidence strongly suggests that a significant impact of climate change is already discernible in animal and plant populations (Root et al. 2003), as well as communities and ecosystems (Walther et al. 2002). For example, analysis of data from the

International Phenological Gardens in Europe has shown that spring events, such as flowering, have advanced by 6 days, and that autumn events have been delayed by 4.8 days when compared with the early 1960s (Menzel and Fabian 1999).

There is now also considerable evidence of impacts of climate change on aeroallergens, particularly pollen (Beggs 2004). Firstly, it appears that plants produce a greater quantity of pollen under these changed climatic conditions. Experimental studies have found substantial increases in pollen production resulting from exposure to increased CO₂ concentration, including from levels equivalent to pre-industrial CO₂ to current concentrations (Wayne et al. 2002; Ziska and Caulfield 2000) (Figure 3). Other studies have examined trends in pollen amount over the latter decades of the 1900s, and found increases to be associated with local rises in temperature (Corden and Millington 2001; Spieksma et al. 1995). Secondly, there is some evidence of significantly stronger allergenicity in pollen from trees grown at increased temperatures (Ahlholm et al. 1998; Hjelmroos et al. 1995). The association between changes in temperature and pollen allergenicity is under investigation, and is likely to vary across plant species. Thirdly, changes in climate appear to have altered the temporal and spatial distribution of pollen. For example, a number of studies have found trends to earlier pollen seasons are associated with local warming over the latter decades of the 1900s (Emberlin et al. 2002; Fitter and Fitter 2002) and recent reports have concluded that the duration of the pollen season is extended in some species (Huynen and Menne 2003). Finally, there are a number of studies that have examined other attributes of allergenic plants, which have also been responsive to CO₂ concentration and/or temperatures increases (e.g. Menzel 2000; Wulff and Alexander 1985). These latter studies provide indirect evidence of impacts of climate change on pollen aeroallergens.

Figure 3 about here

Impacts of climate change on asthma

The links between aeroallergens and allergic diseases such as asthma are well established (Burge and Rogers 2000; Nolte et al. 2001). It is feasible that faster plant growth, earlier plant maturity and longer growing season, plus earlier pollen season, increased season duration and increases in both pollen quantity and allergenicity have already had an impact on asthma, reflected in the global rise in asthma prevalence and increased severity of episodes.

Climate change might readily explain more than just increased morbidity among those with the condition; it could also be a candidate for increasing the initial susceptibility to asthma and hence the prevalence of the condition. Exposure to allergens in infancy is thought to sensitize individuals to asthma (Pearce et al. 2000) and other atopic conditions such as eczema and allergic rhinitis. Björkstén and Suoniemi (1981) found, for example, that exposure to more intense pollen seasons in early infancy increased the likelihood of later development of allergy. Therefore increases in pollen quantity and extended pollen seasons due to climate change may lead to both an increase in the development of the condition and greater morbidity among those who have it (Figure 4).

Figure 4 about here

While future impacts of climate change on human health have received considerable and increasing amounts of attention since the mid-1990s, few studies have documented human health impacts already evident. A study of the El Niño-Southern Oscillation and cholera in Bangladesh from around 1900 to 2001 may provide the first evidence that warming trends over the last century are already affecting human health (Patz 2002; Rodó et al. 2002). The World Health Organization (WHO) has identified climate change as a major environmental

risk to health (WHO 2002). WHO estimated that climate change was responsible for approximately 2.4% of diarrhea cases (worldwide), 6% of malaria cases (in some middle income countries) and 7% of dengue fever cases (in some industrialized countries) in the year 2000. In total, climate change was estimated to be responsible for 0.3% of deaths and 0.4% of Disability Adjusted Life Years (WHO 2002).

The potential for future climate change to have an impact on asthma and other allergic diseases has been recognized for some time (Curson 1993; IPCC 2001), mostly a result of the well-established link between climate and many aeroallergens and aeroallergen-producing organisms, on the one hand, and air pollution on the other. However, that climate change could alter the burden of non-communicable diseases such as asthma has received far less attention than potential impacts on infectious vector-borne and diarrheal diseases.

It is somewhat easier to establish direct links between changing climate and the burden of these infectious diseases, where etiology is fairly well established. In contrast, the etiology of asthma is complex and not well understood. The complexity of asthma, and the greater urgency that tends to be ascribed to communicable disease, may explain why little attention has to date been paid to the effects of climate change on asthma. Furthermore, that climate change impacts on asthma may already be evident has previously not been explored.

Recent urban-rural comparisons in asthma and pollen provide a useful analogy to the global climate change hypothesis presented here. Using the existing CO₂ and temperature gradient between rural and urban areas, Ziska et al. (2003) showed that the higher CO₂ concentrations and air temperatures of urban areas were associated with differences in ragweed (*Ambrosia artemisiifolia*). The urban plants of this established allergy-inducing species produced significantly more pollen than the plants in rural areas. Greater aeroallergen levels in urban

areas may have contributed to the higher childhood asthma prevalence of urban areas. These local effects provide some support for pollen quantity as a significant contributor to asthma prevalence. Weinberg (2000) confirms the urban-rural differences in childhood asthma prevalence, but has shown a much narrower gap, suggesting an accelerated rise in aeroallergen level in rural areas associated with global increases in atmospheric CO₂ concentration and temperature.

Conclusions

Seeking evidence of early effects of climate change on human health has been identified as a major challenge for scientists studying climate change and health (Woodward and Scheraga 2003). The detection of health effects of climate change is necessary as evidence underpinning national and international policies relating to measures to protect public health, such as the mitigation of greenhouse gas emissions (Wilkinson et al. 2003) and, given that we are already committed to some climate change, strategies for adaptation.

Asthma is etiologically complex, with numerous contributing factors and interactive effects within the causal web, many of which are modified by climate. The changing global climate compounds this complexity. There is some evidence to suggest that asthma prevalence – but not severity – may have plateaued in some countries very recently. However, it is too early to determine if this leveling off will be sustained. Either way, the hypothesis that the global rise of asthma is an early impact of anthropogenic climate change still stands. Further, this climate change hypothesis does not conflict with the hygiene hypothesis, but adds an additional possibility to the mix; each may contribute to the observed rise in asthma.

Specific hypotheses relating asthma to climate change must be developed and rigorously tested. To tease out the climate change-asthma relationships, it will be necessary to

distinguish between an increase in the prevalence of asthma and an increase in the morbidity, incidence and burden of disease, as climate change may contribute to both a rise in prevalence and increased severity. Furthermore, because of the variation in prevalence throughout the world, studies will need to address patterns at national, subnational and local scales. Proof that recent climate change has had an adverse impact on asthma will only come from the accumulation of studies focused on this topic. For comparisons of the impact of global climate change between areas and over time, international definitions of asthma, such as that developed by the International Study of Asthma and Allergies in Childhood (ISAAC) (Asher et al. 1995), should be used to establish baselines and to measure trends.

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Figure legends

Figure 1. Changes in asthma point prevalence observed since 1956. NB: The locations used different diagnostic criteria, but these were consistent within each study location. Data from Pearce et al. (2000).

Figure 2. Three-monthly seasonal average atmospheric CO₂ concentration recorded at Mauna Loa Observatory, Hawaii, from March 1958 to December 2002 (data from Keeling and Whorf (2003)). Highest CO₂ occurs in the Northern Hemisphere spring (March, April, May). As this is peak growing season for Northern Hemisphere plants, the higher spring CO₂ levels may further magnify the impact on plant growth and pollen production.

Figure 3. Percentage change in pollen quantities (*Ambrosia artemisiifolia* L.) produced under different concentrations of atmospheric CO₂. Increase in pollen quantity is shown for CO₂ concentrations equivalent to pre-industrial levels (280 ppm), through 1950s levels, to 2000 levels and to potential future levels. Sources: (a) Ziska and Caulfield (2000) and (b) Wayne et al. (2002).

Figure 4. Schematic diagram of the relationship between global climate change and the rise in asthma prevalence and severity, via impacts of climate change on plant and pollen attributes. ↑ Represents increase.

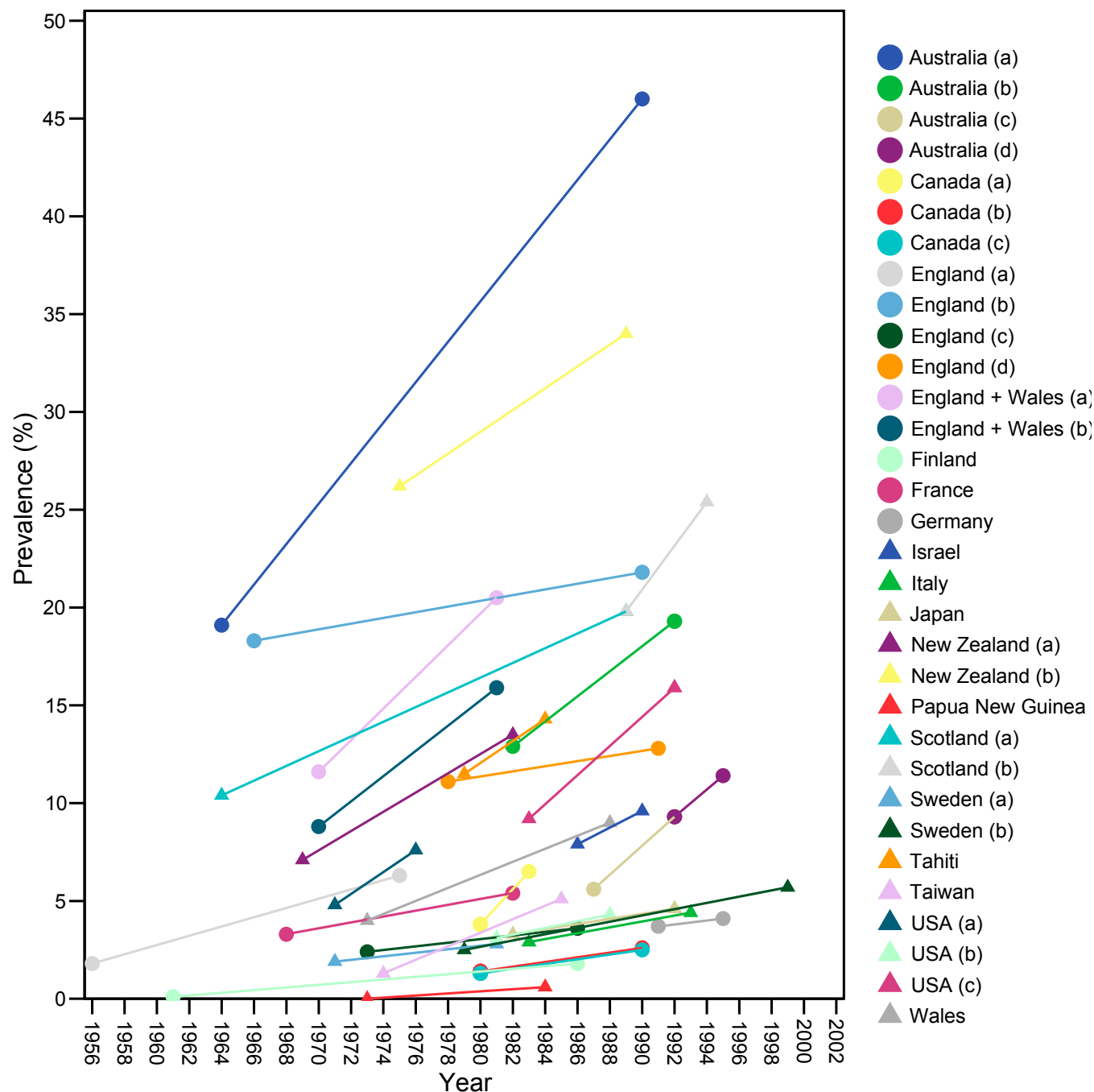


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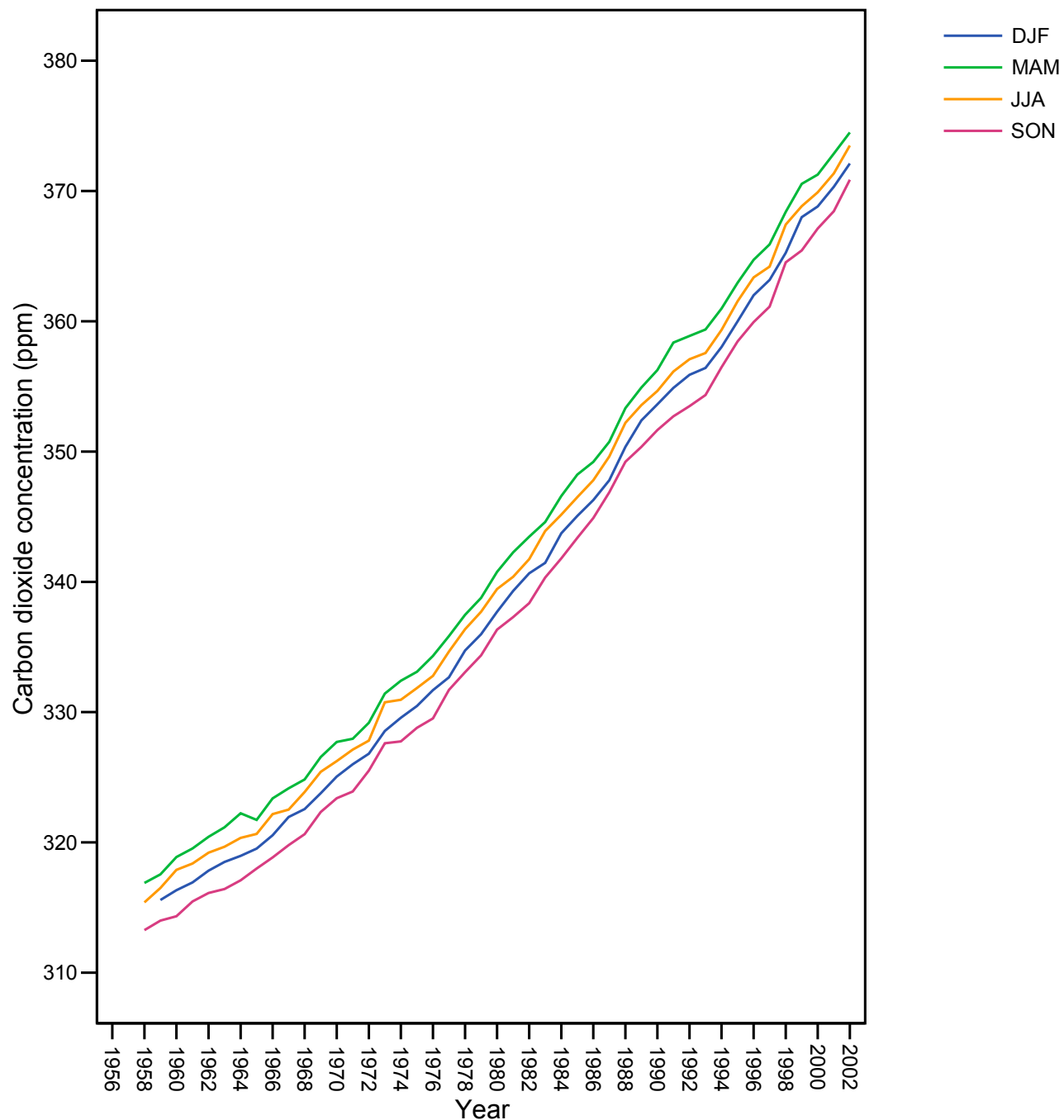


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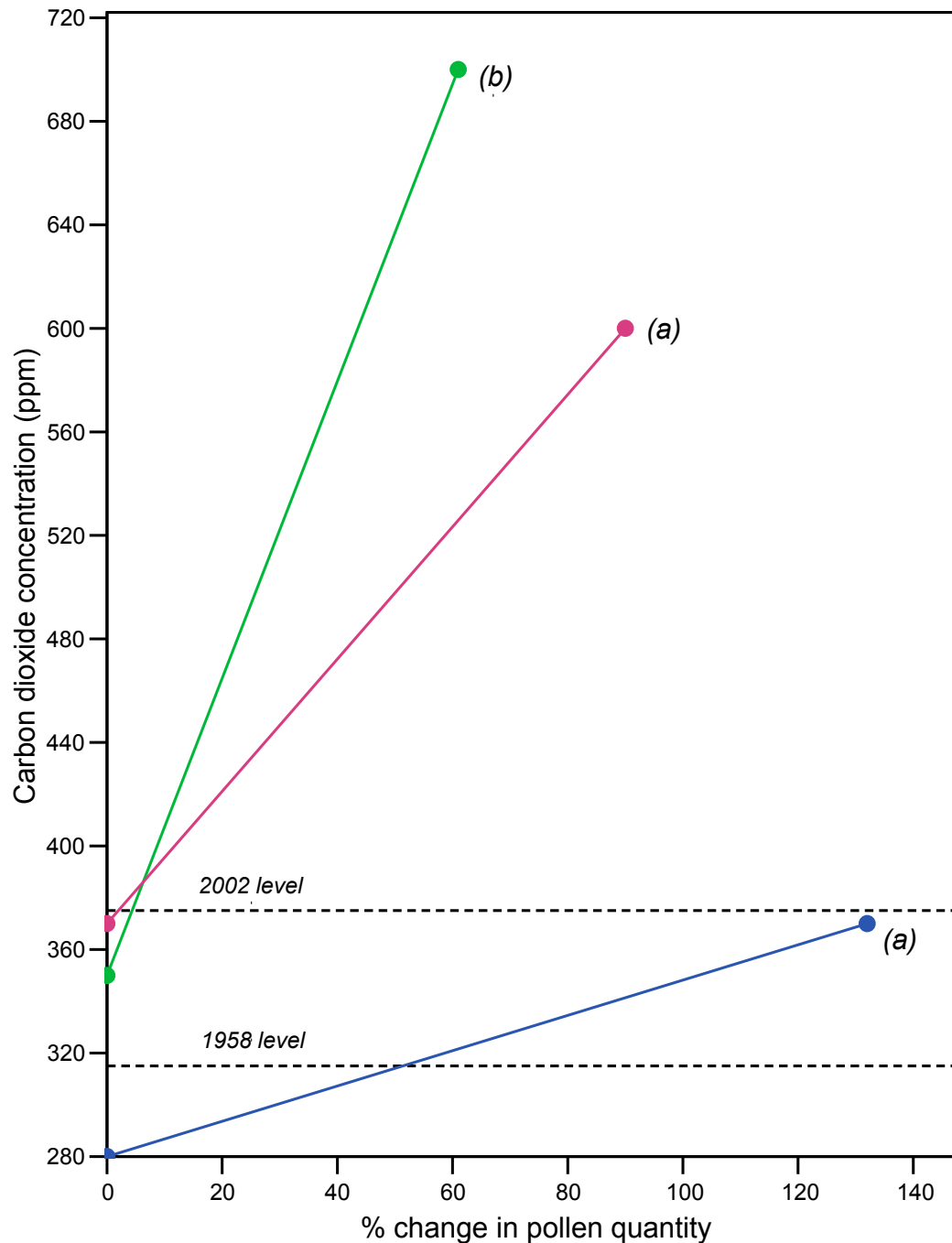


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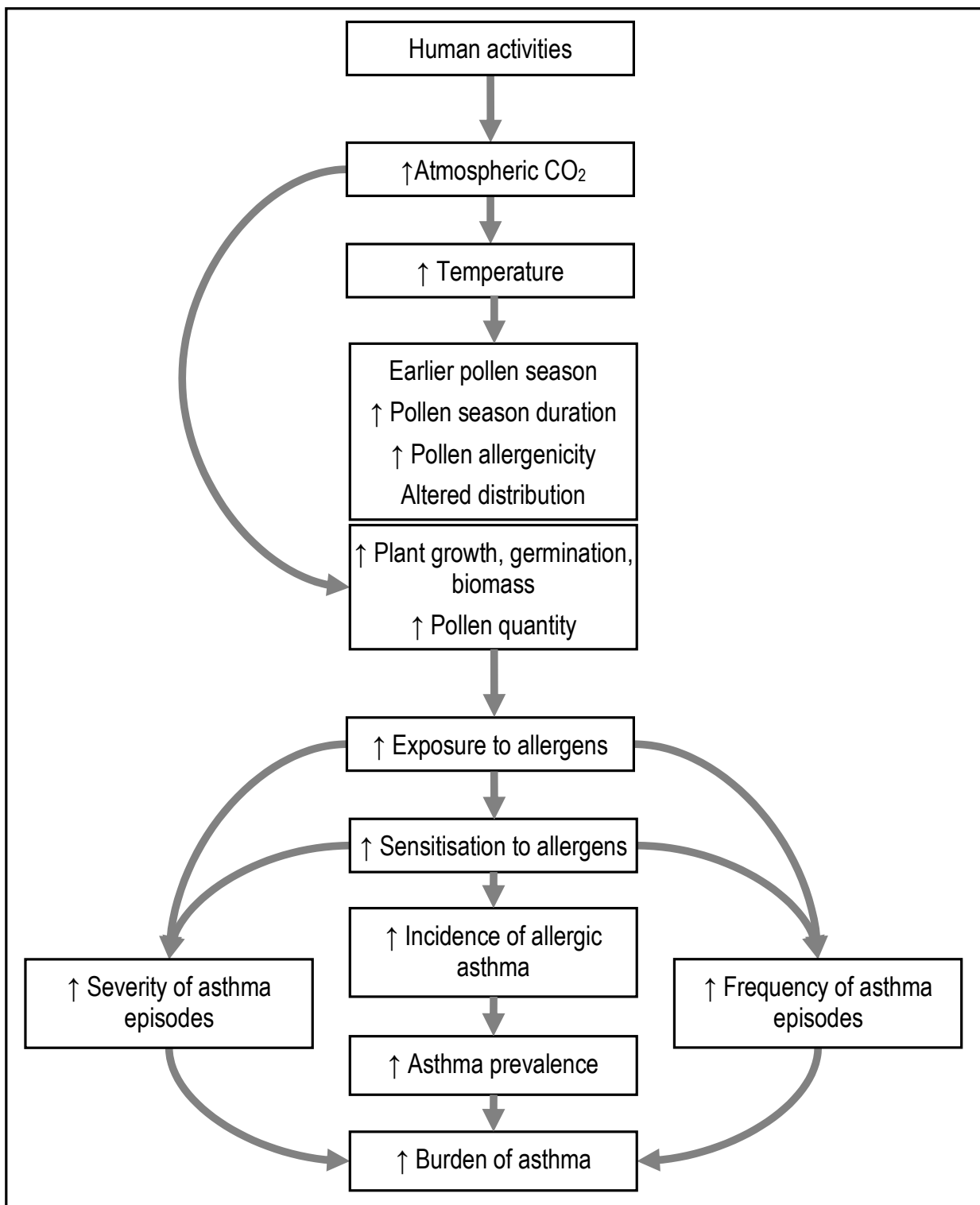


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